WEST

Generate Collection Print

L10: Entry 28 of 67 File: USPT Jan 28, 2003

DOCUMENT-IDENTIFIER: US 6511847 B1
TITLE: Recombinant p53 adenovirus methods and compositions

Other Reference Publication (136):
Ogawa et al., "Novel Combination Therapy For Human Colon Cancer With Adenovirus-Mediated Wild-Type p53 Gene Transfer and DNA-Damaging Chemotherapeutic Agent," Int. J. Cancer, 73:367-370, 1997.

Other Reference Publication (167):
Spitz et al., "Adenoviral mediated p53 gene therapy enhances radiation sensitivity of colorectal cancer cell lines," Proc. Amer. Assoc. Cancer Res., vol. 37, #2366, Mar. 1996.

```
      (FILE 'HOME' ENTERED AT 11:04:08 ON 27 FEB 2003)

      FILE 'MEDLINE, CANCERLIT, EMBASE, BIOSIS, CAPLUS, BIOTECHDS' ENTERED AT
      11:04:25 ON 27 FEB 2003
L1          1982 S ENHANCED GENE EXPRESSION OR INCREASED GENE EXPRESSION
L2       1611107 S ENHANCES OR INCREASES OR FACILITATES
L3       3159128 S AAV OR ADENOVIR? OR PLASMID OR DNA OR NUCLEIC
L4        105196 S L3 AND L2
L5       1703999 S IRRADIATION OR RADIATION OR DNA DAMAGING OR CISPLATIN OR VP16
L6          8692 S L5 AND L4
L7          3448 DUP REM L6 (5244 DUPLICATES REMOVED)
L8             1 S L7 AND L1
L9        157416 S L5 AND L3
L10         8692 S L9 AND L2
L11      3790499 S DAY# OR HOUR#
L12          946 S L11 AND L10
L13       962642 S GENE EXPRESSION OR GENE DELIVERY OR GENE THERAPY
L14          125 S L13 AND L12
L15           61 DUP REM L14 (64 DUPLICATES REMOVED)

=>
```

L15 ANSWER 51 OF 61 MEDLINE DUPLICATE 25
AN 1999035194 MEDLINE
DN 99035194 PubMed ID: 9816114
TI **Adenoviral**-mediated wild-type p53 **gene expression** sensitizes colorectal cancer cells to ionizing **radiation**.
AU Spitz F R; Nguyen D; Skibber J M; Meyn R E; Cristiano R J; Roth J A
CS Departments of Surgical Oncology, Section of Thoracic Molecular Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas 77030, USA.
NC CA 16672 (NCI)
RO1 CA45187 (NCI)
T32-09599-06
SO CLINICAL CANCER RESEARCH, (1996 Oct) 2 (10) 1665-71.
Journal code: 9502500. ISSN: 1078-0432.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990311
Last Updated on STN: 19990311
Entered Medline: 19990225
AB Wild-type p53 gene transfer into the SW620 colorectal carcinoma cell line was performed using the replication-defective **adenovirus** Ad5/CMV/p53 to evaluate the effect of wild-type p53 expression on **radiation** sensitivity. The results indicated that infection with Ad5/CMV/p53 sensitized the cells. The survival at 2 Gy was reduced from 55 to 23%. Flow cytometric analysis of terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling (TUNEL) assay-labeled cells and in situ TUNEL staining of xenograft tumors demonstrated an increase in labeled cells with combination treatment, indicating increased apoptosis in cells treated with Ad5/CMV/p53 before **irradiation**. A significant enhancement of tumor growth suppression by this combination strategy was observed in a s. c. tumor animal model compared to p53 **gene therapy** alone. The delay in regrowth to control tumor size of 1000 mm3 was 2 **days** for 5 Gy, 15 **days** for Ad5/CMV/p53, and 37 **days** for Ad5/CMV/p53 + 5 Gy, indicating synergistic interactions. These data indicate that the delivery of wild-type p53 to cells with p53 mutations **increases** their **radiation** sensitivity, and this may be accomplished by **adenoviral**-mediated **gene therapy**.

L15 ANSWER 50 OF 61 CANCERLIT
AN 97605008 CANCERLIT
DN 97605008
TI **Adenoviral** mediated p53 **gene therapy** **enhances radiation** sensitivity of colorectal cancer cell lines (Meeting abstract).
AU Spitz F R; Nguyen D; Skibber J; Meyn R; Cristiano R J; Roth J A
CS UT M.D. Anderson, Houston, TX 77030.
SO Proc Annu Meet Am Assoc Cancer Res, (1996) 37 A2366.
ISSN: 0197-016X.
DT (MEETING ABSTRACTS)
LA English
FS Institute for Cell and Developmental Biology
EM 199703
ED Entered STN: 19980417
Last Updated on STN: 19980417
AB The p53 tumor suppressor gene has been demonstrated to have a role in cellular response to **radiation**. Mutations in the p53 gene occur in up to 80% of colorectal cancers. These tumors are often treated with multimodality therapy including **radiation**. p53 gene transfer into colorectal carcinoma cell lines with p53 mutations (SW620, SW837, KM12L4) was performed utilizing the replication-deficient **adenovirus** Ad5CMVp53. To evaluate the effect of wild-type p53 expression on **radiation** sensitivity we performed clonogenic survival assays and tumor growth experiments following Ad5CMVp53 infection. The results indicated that infection with Ad5CMVp53 sensitized the cell lines: the survival for the SW620 line at 2 Gy was reduced from 55% to 23%. FACS TdT analysis indicated increased apoptosis in cells treated with Ad5CMVp53 prior to **radiation**. Similar results were seen in the SW837 and KM12L4 cell lines. Subcutaneous SW620 xenografts in nude mice were treated in vivo by direct intratumoral injection of AdCMVp53 followed by 5 Gy **irradiation**. The delay in regrowth to control tumor size of 750 mm3 was 1 **day** for 5 Gy, 10 **days** for Ad5CMVp53, and 24 **days** for Ad5CMVp53 + 5 Gy indicating synergistic interactions. These data indicate that the delivery of wild-type p53 to cells with p53 mutations **increases** their **radiation** sensitivity and this may be accomplished by **adenoviral** mediated **gene therapy**.

L15 ANSWER 44 OF 61 MEDLINE DUPLICATE 21
AN 97470616 MEDLINE
DN 97470616 PubMed ID: 9331076
TI Virally directed cytosine deaminase/5-fluorocytosine **gene therapy enhances radiation** response in human cancer xenografts.
AU Hanna N N; Mauceri H J; Wayne J D; Hallahan D E; Kufe D W; Weichselbaum R R
CS Department of Surgery, Pritzker School of Medicine, University of Chicago, Illinois 60637, USA.
NC CA41068 (NCI)
T32CA09516 (NCI)
SO CANCER RESEARCH, (1997 Oct 1) 57 (19) 4205-9.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971028
AB **Gene therapy** combined with **radiation** therapy to enhance selectively **radiation** cytotoxicity in malignant cells represents a new approach for cancer treatment. We investigated the efficacy of **adenoviral** (Ad5)-directed cytosine deaminase/5-fluorocytosine (CD/5-FC) enzyme/prodrug **gene therapy** to enhance selectively the tumoricidal action of ionizing **radiation** in human cancer xenografts derived from a human squamous carcinoma cell line (SQ-20B). Tumor xenografts grown in hindlimbs of nude mice were transfected with an **adenoviral** vector (Ad.CMV.CD) containing the cytosine deaminase (CD) gene under the control of a cytomegalovirus (CMV) promoter. Mice were injected i.p. with 800 mg/kg of 5-FC for 12 **days**, and tumors were treated with fractionated **radiation** at a dose of 5 Gy/**day** to a total dose of 50 Gy. In larger tumors with a mean volume of 1069 mm3, marked tumor regression to 11% of the original tumor volume was observed at **day** 21 ($P = 0.01$). The volumetric regression of smaller tumors with a mean volume of 199 mm3, which received the same combined treatment protocol, was significant at **day** 12 ($P = 0.014$). However, unlike large tumors, regression of the smaller tumors continued until **day** 36 ($P = 0.01$), with 43% cured at **day** 26. No cures or significant volumetric reduction in size was observed in tumors treated with **radiation** alone; Ad.CMV.CD with or without **radiation**; or with Ad.CMV.CD and 5-FC. These results suggest that the CD/5-FC **gene therapy** approach is an effective radiosensitizing strategy and may lead to substantial improvement in local tumor control that would translate into improved cure rates and better survival.

L15 ANSWER 20 OF 61 MEDLINE DUPLICATE 8
AN 2001523077 MEDLINE
DN 21455490 PubMed ID: 11571017
TI Time-dose relationships in **radiation**-enhanced integration.
AU Stevens C W; Puppi M; Cerniglia G J
CS Department of Radiation Oncology, University of Texas M.D. Anderson Center, 1515 Holcombe Blvd, Houston, TX 77030, USA.. cstevens@mdanderson.org
SO INTERNATIONAL JOURNAL OF RADIATION BIOLOGY, (2001 Aug) 77 (8) 841-6. Journal code: 8809243. ISSN: 0955-3002.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Space Life Sciences
EM 200110
ED Entered STN: 20010926
Last Updated on STN: 20011015
Entered Medline: 20011011
AB PURPOSE: We have shown that ionizing **radiation increases** recombination, as manifested by increased stable transduction of both **plasmid** and **adenoviral** vectors. This paper reports the duration of increased recombination after **irradiation**. MATERIALS AND METHODS: A549 or NIH/3T3 cells were transfected at various times after **irradiation**. Cells were also irradiated with several fractionation schemes and then transfected. RESULTS: Enhanced integration (EI) is a very long-lived process, lasting at least 2-3 **days** after single **radiation** fractions. The duration of EI activation is **radiation** dose-dependent. The efficiency of EI is dependent on **radiation** dose and independent of fractionation, such that low dose-rate, fractionated and single **radiation** doses result in similar levels of EI when corrected for differences in cytotoxicity. CONCLUSIONS: **Radiation**, given with fraction sizes and dose-rates used in clinical **radiation** therapy, induces a long-lived hyper-recombination state. Since radiotherapy is already a component of treatment for many malignancies and is integrated into **radiation -gene therapy** trials, an understanding of recombination events that improve **gene delivery** is important and timely.

WEST

Freeform Search

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Term: l8 with l2

Display: 10 **Documents in Display Format:** - **Starting with Number** 1

Generate: ○ Hit List ◉ Hit Count ○ Side by Side ○ Image

Search | Clear | Help | Logout | Interrupt

Main Menu | Show S Numbers | Edit S Numbers | Preferences | Cases

Search History

DATE: Thursday, February 27, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L10	l8 with l2	67	L10
L9	L8 with l3	2	L9
L8	AAV or adenovir$	19796	L8
L7	L6 with l3	15	L7
L6	enhanced or increased	2208938	L6
L5	L4 with l3	21	L5
L4	facilitate or increase or enhance	3341737	L4
L3	L2 with l1	155	L3
L2	DNA damaging or cisplatin or radiation or ionization	569206	L2
L1	gene expression or gene delivery	35752	L1

WEST

Generate Collection Print

L7: Entry 2 of 15 File: PGPB Sep 5, 2002

PGPUB-DOCUMENT-NUMBER: 20020123477
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020123477 A1

TITLE: Enhanced expression of transgenes

PUBLICATION-DATE: September 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Cristiano, Richard J.	Pearland	TX	US	
Nguyen, Dao	Potomac	MD	US	

US-CL-CURRENT: 514/44; 514/105, 514/34, 514/410, 514/492, 514/589, 514/8

CLAIMS:

1. A method for enhancing the expression of a transgene comprising: (a) contacting a target cell with a DNA-damaging agent; (b) removing said DNA-damaging agent from said target cell; and (c) transferring said transgene into said target cell between about 1-3 days after removing said DNA-damaging agent.

2. The method of claim 1, wherein said target cell is a dividing cell.

3. The method of claim 2, wherein said target cell is a tumor cell.

4. The method of claim 3, wherein said tumor cell is cisplatin sensitive.

5. The method of claim 3, wherein said tumor cell is cisplatin insensitive.

6. The method of claim 1, wherein said DNA-damaging agent is selected from the group consisting of cisplatin, carboplatin; VP16, teniposide, daunorubicin, doxorubicin, dactinomycin, mitomycin, plicamycin, bleomycin, procarbazine, nitrosourea, cyclophosphamide, bisulfan, melphalan, chlorambucil, ifosfamide, merchlorehtamine, and ionizing radiation.

7. The method of claim 1, wherein said transgene is transferred at about 2 days after removing said DNA-damaging agent.

8. The method of claim 1, wherein said transfer of said transgene is accomplished by a technique selected from the group consisting of liposome-mediated transfection, receptor-mediated internalization and viral infection.

9. The method of claim 1, wherein said transgene is a tumor suppressor.

10. The method of claim 9, wherein said tumor suppressor is p53.

11. The method of claim 10, wherein said p53 transgene is under the transcriptional control of a promoter.

12. The method of claim 11, wherein said promoter is the CMV IE promoter.

13. The method of claim 12, wherein said transgene is regulated by a polyadenylation signal.

14. The method of claim 13, wherein said polyadenylation signal is an SV40

polyadenylation signal.

15. The method of claim 14, wherein said p53 transgene is carried in an adenoviral vector.

WEST

Generate Collection Print

L7: Entry 7 of 15 File: USPT Aug 7, 2001

US-PAT-NO: 6271207
DOCUMENT-IDENTIFIER: US 6271207 B1

TITLE: Enhanced expression of transgenes

DATE-ISSUED: August 7, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cristiano; Richard J.	Pearland	TX		
Nguyen; Dao	Potamac	MD		

US-CL-CURRENT: 514/44; 424/93.2, 435/320.1, 435/455, 435/458

CLAIMS:

What is claimed is:

1. A method for enhancing the expression of a transgene in a target neoplastic cell in vivo comprising:

(a) administering a DNA-damaging agent to a subject containing a target neoplastic cell; and

(b) transferring said transgene into said target neoplastic cell between 2-4 days after said administering step;

whereby expression of said transgene is enhanced as a result of the administering of said DNA-damaging agent to said target neoplastic cell.

2. The method of claim 1, wherein said target neoplastic cell is a dividing cell.

3. The method of claim 1, wherein said DNA-damaging agent is selected from the group consisting of cisplatin, carboplatin, VP16, teniposide, daunorubicin, doxorubicin, dactinomycin, mitomycin, plicamycin, bleomycin, procarbazine, nitrosourea, cyclophosphamide, bisulfan, melphalan, chlorambucil, ifosfamide, merchlorehtamine, and ionizing radiation.

4. The method of claim 1, wherein said transgene is transferred at about 3 days after said administering step.

5. The method of claim 1, wherein said transfer of said transgene is accomplished by a technique selected from the group consisting of liposome-mediated transfection, receptormediated internalization and viral infection.

6. The method of claim 1, wherein said transgene encodes a tumor suppressor.

7. The method of claim 6, wherein said tumor suppressor is p53.

8. The method of claim 7, wherein said p53 transgene is under the transcriptional control of a CMV IE promoter.

9. The method of claim 3, wherein said DNA-damaging agent is cisplatin.

10. The method of claim 7, wherein said p53 transgene is carried in an adenoviral vector.

WEST

Generate Collection

L9: Entry 1 of 2 File: PGPB Oct 17, 2002

DOCUMENT-IDENTIFIER: US 20020151060 A1
TITLE: PEI: DNA vector formulations for in vitro and in vivo gene delivery

Detail Description Paragraph (663):
[0705] Spitz et al., "Adenoviral-mediated wild-type p53 gene expression sensitizes colorectal cancer cells to ionizing radiation," Clin. Cancer Res., 2:1665-1671, 1996.

L10: Entry 51 of 67 File: USPT Nov 10, 1998

DOCUMENT-IDENTIFIER: US 5834182 A
TITLE: Method for increasing transduction of cells by adeno-associated virus vectors

Detailed Description Text (36):
Effect of DNA Damaging Agents on Transduction Efficiency of AAV-LAPSN and AAV-L.beta.geo

Detailed Description Text (37):
The following Example shows that DNA damaging agents increase the transduction efficiency of the vectors AAV-LAPSN and AAV-L.beta.geo. The vector AAV-LAPSN contains the human placental alkaline phosphatase gene driven by the Moloney murine leukemia virus LTR promoter and the neo gene driven by the SV40 early promoter. Four agents were tested, ultraviolet light (254 nm), gamma irradiation, tritiated thymidine, and the alkylating agent cis-platinum.

Detailed Description Text (66):
The following study demonstrated that episomal vector DNA amplification does not explain increased transduction. Helper virus-independent amplification of wild-type adeno-associated virus DNA has been reported to occur following genotoxic stress (Yalkdinoglu A. O. et al., Cancer Res. 48, 3124-3129 (1988)). More than 400-fold amplification has been observed in CHO-K1 cells following treatment with the mutagen N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) and a 30-fold amplification in human diploid fibroblasts (E6). To determine whether a similar phenomena might accompany the increased transduction efficiency of AAV vectors in cells exposed to DNA damaging agents, Hirt supernatants from both irradiated and unirradiated cultures of stationary primary human fibroblasts were assayed 48 hours following vector exposure. Quadruplicate cultures received either no treatment, vector alone or both 4000 rad of gamma irradiation and vector. At 48 hours low molecular weight DNA was isolated from triplicate cultures in each treatment group. The fourth culture in each group was stained for alkaline phosphatase-positive cells to determine the increase in transduction efficiency caused by the gamma irradiation, which was in excess of 100-fold. An autoradiograph of low molecular weight DNA isolated from triplicate stationary cultures of primary human fibroblasts in each of three treatment groups was made. The groups were control uninfected cultures, unirradiated cultures infected with AAV-LAPSN and cultures infected with AAV-LAPSN after 4000 rad of gamma irradiation. Briefly, Hirt supernatant DNA, which was harvested from the triplicate cultures from each treatment group 48 hours after infection, was subjected to Southern analysis using a neo probe. A phosphoimager was used to quantitate the total hybridization signal in each lane, and the signal representing the single stranded monomer forms of vector DNA. The maximum variation between lanes was 45% i.e., within experimental error. The results revealed no evidence of significant DNA amplification in gamma irradiated cultures. These data demonstrated that the increased transduction efficiency of AAV vectors in irradiated cells was not due to marked amplification of episomal vector DNA.

L4 ANSWER 12 OF 13 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 1997-04463 BIOTECHDS
TI **Enhancement** of antitumor effects of **p53** gene therapy by combination with **DNA-damaging agents**; adeno virus vector-mediated **p53** tumor suppressor gene transfer together with cisplatin and radiation treatment for enhanced cancer therapy (conference abstract)
AU Harper M E; Cristiano R; Spitz F; Nguyen D; Gjerset R A; Roth J A
CS Introgen-Ther.; Univ.Texas; San-Diego-Reg.Cancer-Cent.
LO Introgen Therapeutics Inc., Houston, TX, USA.
SO Cancer Gene Ther.; (1996) 3, 6, Conf.Suppl., S41-42
CODEN: 2815V ISSN: 0929-1903
Gene Therapy of Cancer, 5th International Conference, San Diego, CA, 14-16 November, 1996.
DT Journal
LA English
AB In order to enhance the effects of **p53** tumor suppressor gene therapy, combinations of adeno virus vector (Ad-**p53**)-mediated gene replacement with **DNA-damaging agents** have been investigated in several in vitro and in vivo models. Cisplatin treatment in combination with Ad-**p53** was found to cause a high degrees of non-small cell lung tumor growth inhibition both in vitro and in vivo, particulary when administered prior to Ad-**p53**. Delivery of Ad-**p53** to colorectal carcinoma cells with **p53** gene mutations significantly increased their radiation sensitivity, again both in vitro and in vivo. Several other tumor cell types expressing endogenous mutant **p53** were also sensitized to DNA-damaging therapies by Ad-**p53**, including glioblastoma (cisplatin and radiation), mamma carcinoma (cisplatin) and prostate carcinoma (cisplatin). This suggests that the approach may have broad application to a wide range of tumor types. These results suggest more effective strategies of gene therapy for malignant disease using combinations of chemo/radiation therapy and **p53** gene replacement. (0 ref)

L7 ANSWER 12 OF 13 MEDLINE DUPLICATE 3
AN 97068009 MEDLINE
DN 97068009 PubMed ID: 8911337
TI **Gene therapy** for **lung cancer**:
enhancement of tumor suppression by a combination of sequential systemic cisplatin and **adenovirus**-mediated **p53** gene transfer.
AU Nguyen D M; Spitz F R; Yen N; Cristiano R J; Roth J A
CS Department of Thoracic Surgery, University of Texas M.D. Anderson Cancer Center, Houston 77030, USA.
NC CA16672 (NCI)
R01 CA45187 (NCI)
R29 CA66037 (NCI)
SO JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, (1996 Nov) 112 (5) 1372-6; discussion 1376-7.
Journal code: 0376343. ISSN: 0022-5223.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961210
AB A more effective gene therapy strategy for lung cancer using sequential cisplatin administration and **adenovirus**-mediated **p53** gene transfer was developed on the basis of our previous observation of enhanced expression of a reporter gene in malignant cells exposed to cisplatin before gene transfer. Transfer of the normal (wildtype) **p53** gene into cisplatin-treated H1299 cells, in which **p53** is homozygously deleted, resulted in up to a 60% further inhibition of cell proliferation in vitro than **p53** transfer into untreated H1299 cells. The cisplatin plus **p53** gene transfer strategy yielded significantly greater apoptosis and tumor growth suppression in an animal model of subcutaneous H1299 tumor nodules than wildtype **p53** gene transfer alone. The timing of cisplatin administration and **p53** gene transfer was shown to be critical: cisplatin administration simultaneous with or subsequent to **p53** gene transfer was less effective than cisplatin-first sequential treatment. Moreover, the in vivo inhibition of tumor growth was maintained by repeated cycles of treatment. This gene therapy strategy has been incorporated into a phase I clinical trial for the treatment of lung cancer and provides a basis for the development of improved therapeutic protocols.

L7 ANSWER 7 OF 13 MEDLINE DUPLICATE 2
AN 2000418671 MEDLINE
DN 20353380 PubMed ID: 10893449
TI Administration of wild-type **p53** adenoviral vector synergistically enhances the cytotoxicity of anti-cancer drugs in human lung cancer cells irrespective of the status of **p53** gene.
AU Inoue A; Narumi K; Matsubara N; Sugawara S; Saijo Y; Satoh K; Nukiwa T
CS Department of Respiratory Oncology and Molecular Medicine, Institute of Development, Aging, and Cancer, Tohoku University, Sendai, Japan.
SO CANCER LETTERS, (2000 Aug 31) 157 (1) 105-12.
Journal code: 7600053. ISSN: 0304-3835.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000907
AB Recombinant **adenovirus** mediated **p53** gene transfer combined with anti-cancer drugs has clinical potential for **gene therapy** of **lung cancer**. We constructed a recombinant adenoviral vector expressing wild-type **p53** cDNA (Ad-**p53**), and assessed the efficacy of a combined treatment with Ad-**p53** and six anti-cancer drugs (cisplatin, 5-fluorouracil, doxorubicin, docetaxel, irinotecan, and etoposide) for human lung cancer cell lines, H1299 (with deleted **p53**), RERF-LC-OK (with mutant **p53**), and A549 (with wild-type **p53**). The infection of the Ad-**p53** vector into H1299 cells, RERF-LC-OK cells, or A549 cells increased the sensitivity to all six drugs regardless of the cellular **p53** status, and a synergism was observed by the isobolic method in combination studies (D<1). We conclude that our strategy using adenoviral mediated **p53** gene transfer to cancer cells can enhance the cytotoxic effect of anti-cancer drugs, which leading to an improvement of lung cancer chemotherapy.

L7 ANSWER 11 OF 13 CANCERLIT
AN 97605011 CANCERLIT
DN 97605011
TI **Gene therapy** for **lung cancer**: enhancement of tumor suppression by a combination of systemic cisplatin and **adenovirus**-mediated **p53** gene transfer (Meeting abstract).
AU Nguyen D; Wiehle S; Koch P; Roth J A; Cristiano R
CS Section of Thoracic Molecular Oncology, Dept. of Thoracic and Cardiovascular Surgery, Univ. of TX M.D. Anderson Cancer Center, Houston, TX 77030.
SO Proc Annu Meet Am Assoc Cancer Res, (1996) 37 A2370.
ISSN: 0197-016X.
DT (MEETING ABSTRACTS)
LA English
FS Institute for Cell and Developmental Biology
EM 199703
ED Entered STN: 19980417
Last Updated on STN: 19980417
AB Restoration of the wild-type **p53** status by gene replacement therapy in cancer cells carrying an abnormal **p53** gene leads to cell arrest in G1 phase and/or apoptosis. We identified that brief exposure of lung cancer cell line H1299 to low doses of cisdiamminedichlorocisplatin (CDDP) resulted in 2-2.5 fold elevation of transgene expression. The **p53**-negative H1299 cells were incubated with CDDP prior to transfection with Adv/CMV/**p53** at MOIs of 1 or 5. CDDP-treated cells had 35% (MOI = 1) to 61% (MOI = 5) further inhibition of growth 3 days following **p53** gene transfer compared to cells without prior CDDP treatment. In vitro Adv/CMV/**p53** transfection of CDDP-treated cells led to earlier and higher levels of **p53** gene expression as well as increased apoptosis. Using H1299 subcutaneous tumors (200 mm3) in nude mice, a combination of sequential ip CDDP and intratumoral injections of Adv/CMV/**p53** given 2,4,6 days following ip CDDP resulted in a profound inhibition of tumor growth. While ip CDDP had minimal effect on H1299 tumor growth; tumors treated by this combination were significantly smaller than those treated with Adv/CMV/**p53** alone. The timing of ip CDDP relative to gene transfer is critical as simultaneous ip CDDP and intratumoral AdV/CMV/**p53** injections resulted in a lower therapeutic efficacy. A second cycle of therapy given 10 days after completion of the first one led to further suppression of tumor growth. In conclusion, the combination of sequential ip CDDP and intratumoral injection of AdV-CMV-**p53** enhanced tumor growth inhibition and can be maintained by repeated cycles. This gene therapy strategy is now being tested in a phase I clinical trial of **gene therapy** for **lung cancer**.

L2 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:488172 BIOSIS
DN PREV200000488293
TI Autosomal dominant hypophosphatemic rickets (ADHR) is caused by mutations in a gene encoding a novel member of the fibroblast growth factor family (**FGF-21**.
AU Lorenz-Depiereux, B. (1); White, K. E.; Evans, W. E.; Speer, M. C.; O'Riordan, J. L. H.; Meitinger, T. (1); Econs, M. J.; Strom, T. M. (1)
CS (1) Medizinische Genetik, Ludwig-Maximilians-Universitaet, Muenchen Germany
SO American Journal of Human Genetics, (October, 2000) Vol. 67, No. 4 Supplement 2, pp. 12. print.
Meeting Info.: 50th Annual Meeting of the American Society of Human Genetics Philadelphia, Pennsylvania, USA October 03-07, 2000 American Society of Human Genetics
. ISSN: 0002-9297.
DT Conference
LA English
SL English